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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,665	12/13/2005	Angela Basilio	21376YP	2299
210	7590	09/18/2009	EXAMINER	
MERCK AND CO., INC			GOON, SCARLETT Y	
P O BOX 2000				
RAHWAY, NJ 07065-0907			ART UNIT	PAPER NUMBER
			1623	
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			09/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/560,665	BASILIO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 22 June 2009.

2a) This action is **FINAL**.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-8 is/are pending in the application.

4a) Of the above claim(s) 5,6 and 8 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-4 is/are rejected.

7) Claim(s) 7 is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date <u>13 December 2005</u> .	6) <input type="checkbox"/> Other: _____ .

## DETAILED ACTION

Claims 1-8 are pending in the instant application.

### ***Priority***

This application is a National Stage entry of PCT/US04/23780 filed on 20 July 2004 and claims priority to U.S. provisional application no. 60/489865 filed on 24 July 2003.

### ***Election/Restrictions***

Applicant's election of Group I, claims 1-4 and 7, drawn to a compound of structural formula (I) and a process for the preparation of said compound, in the reply filed on 22 June 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5, 6 and 8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 22 June 2009.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-4 and 7 will be examined on its merits herein.

***Information Disclosure Statement***

The information disclosure statement (IDS) dated 13 December 2005 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits.

***Claim Objections***

Claims 1, 2 and 7 are objected to because they include reference characters which are not enclosed within parentheses.

Reference characters corresponding to elements recited in the detailed description of the drawings and used in conjunction with the recitation of the same element or group of elements in the claims should be enclosed within parentheses so as to avoid confusion with other numbers or characters which may appear in the claims. See MPEP § 608.01(m). For example, instantly recited “formula I” should be indicated as “formula (I)”.

Claim 2 is also objected to because of the following informalities: The font for “sp.” in “*Streptomyces* sp.” should not be italicized. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the preparation of a compound of structural formula (I) which comprises the cultivation of ATCC #PTA-5316 and ATCC #PTA-5317 or a natural strain of *Streptomyces* sp., does not reasonably provide enablement for a method for the preparation of a compound of structural formula (I) which comprises the cultivation of any artificial mutant of a *Streptomyces* sp. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn to a process for the preparation of a compound of structural formula (I) which comprises cultivation of an artificial mutant of a *Streptomyces* sp.

Breadth of claims: The claims are broader than the disclosure. Specifically, they encompass any artificial mutant of a *Streptomyces* sp.

State of the prior art/Predictability or unpredictability of the art/Relative skill of those in the art: Methods for the generation of bacterial mutants are known in the art. However, as taught by Karsi *et al.* (PTO-892, Ref. U), “a major hurdle in identifying bacterial mutants...is that the screening methods tend to be labor intensive” (p. 2166, column 1). Although random mutations can be generated rather quickly, the evaluation of each mutant to determine where the mutation occurred and what properties it possesses or no longer possesses is laborious (Hensel *et al.*, PTO-892, Ref. V; p. 1050, Table 1).

The level of skill of the art involves screening *in vitro* and/or *in vivo* to determine which strains exhibit the desired properties. There is no absolute predictability even in view of the seemingly high level of skill in the art that the desired mutant would be obtained and that the mutation does not affect other aspects of the bacteria. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any mutant on its face, without evidence to support that particular mutant.

With the limited direction and exemplification the specification offers, it is highly unpredictable that said artificial mutants will actually be useful for producing the

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compound of structural formula (I). The evidence supports the conclusion that the method of producing the instantly claimed compound from an artificial mutant is a subject for further study and experimentation.

Therefore, for the reasons above, the state of the prior art is one of unpredictability.

Amount of guidance/Existence of working examples: A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the strains which fall within the scope of a claim will possess the alleged activity of producing the compound. The specification does not adequately enable a method of preparing the compound of structural formula (I) that is encompassed by the claimed method.

There is only data present for the production of the compound of structural formula (I) from MA 7327 and MA7331. Although Applicants indicate that artificial mutants can be obtained by conventional, physical or chemical mutagens, there are no working examples in the specification for the preparation of artificial mutants.

As discussed above, it would be necessary for Applicant to provide evidentiary support for each embodiment due to the unpredictability in the art with regards to the success of some mutants over others.

Lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable art. See MPEP § 2164.

Quantity of experimentation necessary: While the level of skill in the pharmaceutical arts is high, it would require undue experimentation for one of ordinary skill in the pertinent art to prepare artificial mutants of said *Streptomyces* sp.

The quantity of experimentation needed to make the artificial mutants encompassed by the claims would be an undue burden on one skilled in the art for the reasons stated above.

*Genetech*, 108 F.3d at 1366, states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the *Wands* factors as discussed above, e.g., the amount of guidance provided, the predictability of the art and the lack of working examples, to practice the claimed invention herein, a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success. This discussion has established *prima facie* non-enablement.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. As disclosed by Applicants, the compound of structural formula (I) is a natural product of the *Streptomyces* sp. In the absence of the

hand of man, e.g. as in an isolated product, the natural product is considered non-statutory subject matter.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by journal publication by Kanbe *et al.* (PTO-892, Ref. W), as evidenced by Singh *et al.* (PTO-892, Ref. X).

Kanbe *et al.* disclose the isolation of a compound known as AB3217-A from the fermentation broth of a strain of *Streptomyces platensis* (p. 458, abstract; p. 458, first paragraph). The strain, identified as *Streptomyces platensis* AB3217, was isolated from a soil collected in Japan. Kanbe *et al.* disclose that the *Streptomyces platensis* strain is cultured at 27 °C for 72 hours (p. 459, paragraph 1). The culture broth was filtered and the filtrate was purified on an Amberlite column to obtain the active principle (p. 460, subheading "Isolation").

It is noted that Kanbe *et al.* do not explicitly disclose that their strain of *Streptomyces platensis* produces the instantly claimed compound of structural formula (I). However, as Applicants' instant Specification teaches that the instantly claimed compound is a natural product produced by the *Streptomyces* species, and that other

natural strains of the *Streptomyces* species can be used insofar as they can produce the instantly claimed compound, and Singh *et al.* indicate that the MA7327 and MA7331 strains used by Applicants are of the *Streptomyces platensis* taxonomy, it is the Office's position that the *Streptomyces platensis* strain taught by Kanbe *et al.* also necessarily produces the instantly claimed compound of structural formula (I) as the strain taught by Kanbe *et al.* belongs to the same genus and species as that of the strains taught by Applicants. When, as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). It is incumbent upon the applicant to provide evidence or comparative data to the contrary. Furthermore, it is the Office's position that the filtrate would necessarily comprise the claimed compound and suffice as a pharmaceutical composition comprising the instantly claimed compound.

Thus, *Streptomyces platensis* AB3217, taught by Kanbe *et al.*, anticipates claims 1-4 and 7.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/  
Supervisory Patent Examiner, Art Unit 1623

SCARLETT GOON  
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